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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/919,102

07/31/2001

Howard Fein

HOFE / 02

2446

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05/27/2005

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EXAMINER

WITZ, JEAN C

ART UNIT

PAPER NUMBER

1651

DATE MAILED: 05/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action  
Before the Filing of an Appeal Brief**

Application No.

09/919,102

Applicant(s)

FEIN, HOWARD

Examiner

Jean C. Witz

Art Unit

1651

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 28 February 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.  
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**NOTICE OF APPEAL**

2. ☐ The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

**AMENDMENTS**

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);  
(b) ☐ They raise the issue of new matter (see NOTE below);  
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

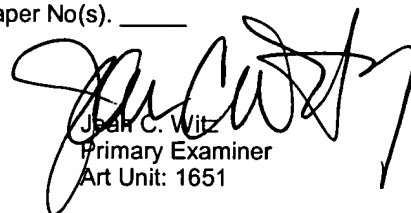
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
5. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.  
6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
The status of the claim(s) is (or will be) as follows:  
Claim(s) allowed: none.  
Claim(s) objected to: none.  
Claim(s) rejected: 1,2,4,5,8,9,24,25,30,31,34,35,37-40 and 43.  
Claim(s) withdrawn from consideration: \_\_\_\_\_.

**AFFIDAVIT OR OTHER EVIDENCE**

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

**REQUEST FOR RECONSIDERATION/OTHER**

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: please see attached document.  
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). \_\_\_\_\_.  
13. ☐ Other: \_\_\_\_\_.

  
Jean C. Witz  
Primary Examiner  
Art Unit: 1651

PD

## DETAILED ACTION

### *Response to Amendment*

1. The amendment filed February 28, 2005 has been entered.

### *Response to Arguments*

2. Applicant's arguments filed February 28, 2005 have been fully considered but they are not persuasive for the reasons set forth below.

Applicant "questions the propriety of making the previous action final." Applicant asserts that the previous office action did not specifically "assert" anticipatory teachings and this was improper and that the Examiner was required to show the particular part of the reference relied upon in the office action.

Applicant's attention is directed to 37 C.F.R. 1.104(c)(2) which states:

In rejecting claims for want of novelty or for obviousness, the examiner must cite the best references at his or her command. When a reference is complex or shows or describes inventions other than that claimed by the applicant, the particular part relied on must be designated as nearly as practicable. The pertinence of each reference, if not apparent, must be clearly explained and each rejected claim specified. (Emphasis added.)

As interpreted by the MPEP 7.06.02(i), the term "clearly anticipates" is properly used in a rejection when the references are explicit on their face that they meet each and every limitation of the claims, and no further explanation is necessary. Applicant's attention is directed to the fact that at the time of the preparation of the previous two office actions, only the abstract of the SU document was available. As a result, the

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Examiner deems that, per 37 C.F.R. 1.104(c)(2), the reference was not "complex" such that the particular part relied upon and the pertinence of the reference to the rejection were "apparent" and explicit on its face; as indicated by the rule, no further explanation was either necessary or required. Applicant's continued argument of the impropriety of the finality of the previous office action remains unpersuasive for these reasons.

Applicant is advised that the translation of the SU document has since become available and is enclosed with this office action.

Applicant's argument that the enzyme is the sole active ingredient remains unpersuasive for the following reasons. The statements of the specification identified as evidence of this intention provide no basis for such a conclusion. In fact, Applicant's citation of the specification at page 18, lines 14-18 provides evidence that the enzyme was not intended to be the sole active ingredient, since the specification states that "The composition containing an enzyme or mixture of enzymes may also contain other compounds that have desirable therapeutic, cosmetic, and/or aesthetic properties . . . ." The only proscription is that the extra ingredients do not affect or only minimally affect the activity of the enzyme. Any of the disclosed "therapeutic, cosmetic, and/or aesthetic properties" of the extra ingredients are clearly "active" in that they have specific and desired effects. It remains unclear how Applicant can argue otherwise. Regardless of this assertion, the proper test of whether any given ingredient of a prior art composition is excluded when claims recite the transitional phrase "consisting essentially of" is whether the ingredient "affect[s] the basic and novel characteristics" of the claimed

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invention. In re Herz, 537 F.2d 549, 551-52, 190 USPQ 461, 463 (CCPA 1976) (emphasis in original).

Applicant argues that because theophylline is a drug, it is an “active” ingredient having pharmacological activities. Applicant cites Goodman and Gilman, The Pharmacologic Basis of Therapeutics” which states that theophylline is a methylxanthine and that methylxanthines have three basic cellular actions: 1) cellular actions “associated with translocations of intracellular calcium, 2) cellular actions “mediated by increasing accumulation of cyclic nucleotides, and 3) cellular actions mediated by blockage of receptors for adenosine. Applicant asserts that these pharmacological activities “would materially affect the basic and novel characteristics of the claimed invention at least because of its effect on the above described calcium translocation, cyclic nucleotides, and receptive blocking properties processes.” (Emphasis in original.)

However, other than citing generic “cellular actions” having the three enumerated effects, Applicant provides no disclosure or explanation of how theophylline materially affects the activity of trypsin on seborrheic keratosis, or even the effect of theophylline on the skin in general. The activity of trypsin on the skin is well known, as evidenced by U.S. Patent 6,440,437 to Krzysik et al., which states that trypsin is an enzyme found in feces which causes skin irritation when the feces contact skin. U.S. Patent 6,623,959 to Harris shows that when trypsin is applied to the epidermis, the epidermal tissue is digested, and the individual epidermal cells are dissociated from their normal organization as epidermal tissue. This clearly explains the irritating nature of trypsin

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when placed on the epidermis. Applicant's attention is drawn to prior art U.S. Patent 3,957,994 to Schroer, U.S. Patent 4,208,406 to Lapinet et al., and U.S. Patent 6,051,602 to Bissett. Each of these patents disclose the pharmacological activity of theophylline when applied to the skin in the treatment of various conditions. None of these patents show that theophylline, when applied to the skin, provides any similar effect on the epidermis. In fact, in U.S. Patent 3,957,994 to Schroer, theophylline is disclosed as being anti-inflammatory when applied to inflamed skin (where trypsin can only be described as being inflammatory when applied to skin). Similarly, U.S. Patent 4,208,406 to Lapinet et al. teaches that theophylline decreases the inflammation produced by skin scalding. See Table 2, Treatment (D). U.S. Patent 6,051,602 to Bissett discloses theophylline as an anti-cellulite agent (col. 7, lines 11-12). As a result, it can reasonably concluded that theophylline has no material effect on the activity of the trypsin; it is not a trypsin inhibitor nor is it a trypsin synergist.

Applicant's assertion that that the '612 patent does not disclose a hydrolase that is "selective for a layer of the skin." However, Applicant admits that the '612 patent specifically states that the multifunctional enzyme has at least one of a chymotrypsin, trypsin, elastase, collagenase, or exopeptidase activity. As discussed supra, enzymes with chymotrypsin or trypsin activity would inherently have an effect on the epidermis. Enzymes having elastase, collagenase, or exopeptidase activity would inherently have an effect on the dermis, since elastin, collagen and other proteins are found in the dermis. All of these enzymatic activities are inherently hydrolases. The patent teaches the use of this enzyme in the treatment of acne, a skin condition found in the epidermis

and the dermis. Therefore, the '612 patent inherently discloses method of treating skin using a hydrolase. Applicant has deleted the phrase "selective for a layer of skin affected by said condition" from the claims; therefore, it remains unclear why Applicant continues to argue that such a limitation is required, even notwithstanding the fact that if the enzyme has trypsin activity, it will act as trypsin and therefore will inherently be "selective for a layer of the skin" as Applicant discloses trypsin to be such an enzyme.

With regard to Applicant's mere assertion that the amendments requiring topical or injectable administration render the published application to Freeman non-obvious, Applicant's arguments fail to comply with 37 CFR 1.111(b) because they amount to a general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references. However, if Applicant is asserting that the amendment includes a limitation not taught or suggested by Freeman, it is respectfully submitted that Freeman topically applies trypsin to in vivo skin tissue to treat skin lesions, specifically by "streaming a solution containing an effective amount of at least one protease, over, and in contact with, the skin portion." Broadest reasonable interpretation of the term "topical application" in the claim includes the treatment of the Freeman document because the enzyme is brought in contact with the skin portion by directing the enzyme topically to the skin surface.

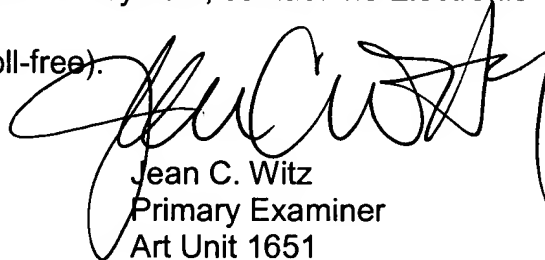
Therefore, Applicant's arguments have been individually addressed and found to lack persuasiveness. The rejections of record are properly maintained.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jean C. Witz whose telephone number is (571) 272-0927. The examiner can normally be reached on 6:30 a.m. to 4:00 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Jean C. Witz  
Primary Examiner  
Art Unit 1651